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INVITED RESEARCH HIGHLIGHT

Prostate Cancer

Robotic radical prostatectomy in high-risk prostate cancer: current perspectives

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Around 20%–30% of patients diagnosed with prostate cancer (PCa) still have high-risk PCa disease (HRPC) that requires aggressive treatment. Treatment of HRPC is controversial, and multimodality therapy combining surgery, radiation therapy, and androgen deprivation therapy have been suggested. There has been a trend toward performing radical prostatectomy (RP) in HRPC and currently, robot-assisted laparoscopic RP (RARP) has become the most common approach. Number of publications related to robotic surgery in HRPC is limited in the literature. Tissue and Tumor characteristics might be different in HRPC patients compared to low-risk group and increased surgical experience for RARP is needed. Due to the current literature, RARP seems to have similar oncologic outcomes including surgical margin positivity, biochemical recurrence and recurrence-free survival rates, additional cancer therapy needs and lymph node (LN) yields with similar complication rates compared to open surgery in HRPC. In addition, decreased blood loss, lower rates of blood transfusion and shorter duration of hospital stay seem to be the advantages of robotic surgery in this particular patient group. RARP in HRPC patients seems to be safe and technically feasible with good intermediate-term oncologic results, acceptable morbidities, excellent short-term surgical and pathological outcomes and satisfactory functional results.

Prostate cancer (PCa) accounts for almost 30% of all newly diagnosed cancers in men in the United States and is the second most frequent cause of cancer death in men.[1] Due to serum prostate specific antigen (PSA) screening, there is an increase in the percent of patients diagnosed with localized PCa.[2] However, around 20%–30% of patients diagnosed with PCa still have high-risk, nonmetastatic disease.[3]

In 1998, D'Amico *et al.* first proposed a three-group risk stratification system to predict posttreatment biochemical failure following radical prostatectomy (RP) and external-beam radiotherapy.[4] This system classified nonmetastatic PCa into low-, intermediate- and high-risk PCa according to initial serum PSA, clinical T stage and biopsy Gleason score (**Table 1**). Low-risk PCa was defined as 1992 AJCC T1/T2a, and PSA ≤10 ng ml^{-1}, and Gleason score ≤6. Intermediate-risk PCa was defined as 1992 AJCC T2b, and/or PSA 10–20 ng ml^{-1} and/or Gleason 7 disease. High-risk PCa (HRPC) was classified as having any one of the following features including 1992 AJCC ≥T2c, PSA >20 ng ml^{-1} or Gleason 8–10 disease.[4] On the other hand, Loeb *et al.* defined HRPC using two definitions including: (*i*) 1992 TNM of cT2b and biopsy Gleason score 8–10, or PSA ≥15 ng ml^{-1}, and (*ii*) those with 1992 TNM of cT3.[5]

Aggressive treatment is required in HRPC otherwise this disease might progress and cause serious symptoms and complications and eventually patient death.[6] Although treatment of HRPC is controversial, radiation therapy, androgen deprivation therapy, surgery and most importantly multimodality therapy combining surgery and radiation have been suggested in various studies[7,8] meaning that RP could only cure a percentage of this patient group.[9–11] The outcomes of the Swedish Registry Study that has been very recently published suggested that surgery seems to be superior to radiation therapy and longer cancer-specific survival (CSS) was achieved in the surgery group in patients with HRPC as per a 15-year CSS data.[12] Therefore, there has been a trend toward performing RP in HRPC patients.[13]

Although open RP (ORP) is a well-established and standard surgical technique in the surgical management of patients with PCa, robotic approach has become the most common approach for PCa surgery in USA.[14] Many authors have published their outcomes related with robot-assisted laparoscopic RP (RARP) with promising results particularly in low- and intermediate-risk PCa patients with similar oncological and functional outcomes to open surgery suggesting the advantages of decreased blood loss, shorter duration of hospital stay, decreased postoperative analgesic requirement and earlier convalescence in the robotic surgery group.[15–18] On the other hand, the number of publications related to the use of robotic surgery in HRPC is very limited in the literature. They mostly have limited numbers of patients and short follow-up periods. Herein, we summarized the literature on RARP and HRPC.

TECHNIQUE OF ROBOT-ASSISTED RADICAL PROSTATECTOMY

We previously reported our technique of RARP using the da Vinci-S surgical system (Intuitive Surgical, Sunnyvale, CA, USA).[19] We use a transperitoneal approach and place a total of 5 abdominal ports We avoid using electrocautery particularly at the tip of the seminal vesicles (SVs) in order not to damage the neurovascular bundles (NVBs) and use nonabsorbable endoclips.

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Table 1: Classification of nonmetastatic PCa into risk groups by D'Amico *et al.* according to initial serum PSA, clinical T stage and biopsy Gleason score[4]

Risk group	*Clinical T stage*	*Serum PSA (ng ml^{-1})*	*Biopsy Gleason score*
Low-risk	1992 AJCC T1/T2a	≤10	≤6
Intermediate -risk	1992 AJCC T2b	10–20	7
High-risk	1992 AJCC≥T2c	>20	8–10

PSA: prostate specific antigen

Bilateral extended pelvic lymph node dissection (ePLND) is performed in intermediate- or high-risk PCa patients and in those with an at least 5% risk of pelvic LN involvement by PCa according to Partin's tables.[20]

Overall, our positive surgical margin ((+) SM) rate was 20% (6.7% in pT2 and 32.4% in pT3 disease). Of the patients, 82.9% had urinary control at the 3-month follow-up. Regarding patients with preoperative International Index of Erectile Function (IIEF) scores ≥19 (mean: 47.6, $n = 46$), mean IIEF score was 45.3 ($n = 11$) at the 9-month follow-up. Regarding patients with preoperative IIEF scores of 13–18 (mean: 16.3, $n = 6$), mean IIEF score was 17.0 ($n = 3$) at the 9-month follow-up.[19]

Tewari *et al*. prospectively evaluated outcomes of radical retropubic and robotic RP procedures.[17] They concluded that robotic RP was safer, less bloody and required shorter duration of hospital stay and urethral catheterization. In addition, they stated that the oncological and functional results were favorable in the robotic RP group.[17]

IMPORTANT SURGICAL TECHNICAL FEATURES IN HIGH-RISK PATIENTS DURING ROBOT-ASSISTED RADICAL PROSTATECTOMY

We suggest gaining sufficient surgical experience in low-risk cases before proceeding to perform advanced high-risk cases because there is a risk of losing tissues of dissection in advanced cases, and anatomic variations might be present. In robotic surgery, because we do not have the tactile sensation, we need to see the anatomical details very well and also know the anatomy in detail. In addition, bulky disease and involvement of SVs and bladder neck by PCa could make dissection during RARP more difficult.[21]

It has been suggested that HRPC may be associated with firm SVs that might suggest tumor invasion and necessitates careful manipulation of the tissues in order to completely remove with negative SMs ((−) SMs).[21] Following opening the Denonvillier's fascia, meticulous dissection should be done between the plane of rectum and prostate. In advanced cases, characterization of this plane might be difficult due to the presence of extra-capsular disease and in patients with previous androgen deprivation therapy.[21] It is important to keep in mind that wide dissection and resection might lead to rectal injury particularly in patients with extra-capsular disease. On the other hand, dissecting as close as up to the apex between the plane of prostate and rectum following opening the Denonvillier's fascia significantly facilitates the procedure.

Another important area of dissection is the plane between the bladder neck and prostate base. Some authors suggested avoiding the natural tendency to advance toward the prostate and use a perpendicular place of dissection between the bladder neck and prostate base in order to prevent a (+) SM. In case of suspicion, intraoperative frozen section analysis could also be useful.[22,23]

Tewari *et al*.[24] suggested that defining periprostatic fascial planes, color and tissue characteristics, presence of inflammatory changes and adhesions and determination of freely separating bloodless plane showing loose shiny areolar tissue as visual clues to decrease the risk of posterior-lateral (+) SMs.

Stroup and Kane suggested meticulous circumferential dissection of the prostate apex in order to avoid (+) SMs.[21]

In summary, tissue characteristics might be different in HRPC patients during RARP that needs increased surgical experience.

PRESERVATION OF NEUROVASCULAR BUNDLES IN HIGH-RISK PATIENTS DURING ROBOT-ASSISTED RADICAL PROSTATECTOMY

In our surgical approach, we perform interfascial or intrafascial NVB preservation on the nontumor bearing prostate side and non-NVB sparing wide excision of the tumor-bearing side in HRPC patients during performing RARP. Although the lack of tactile feedback related with robotic surgery is a concern, intraoperative tissue characteristics affect our decision and type of NVB sparing in this patient group. In the presence of adherent periprostatic tissue or extensive adhesions and inability to define periprostatic fascial planes that might suggest extra-capsular disease, we do not perform NVB-sparing. Likewise, other authors suggested considering extrafascial or modified nerve sparing approach with medial endopelvic fascia incision in an attempt to balance surgical oncologic control with functional outcomes.[21]

Lavery *et al*. reported the outcomes of 123 high-risk patients with preoperative HRPC diagnosis. Of the patients, bilateral, unilateral, and nonnerve-sparing was performed on 58%, 15%, and 27%, respectively.[25] Poorly defined planes, bulging of the capsule and appearance of prostatic tissue on the NVBs were suggested as possible risk factors for NVB involvement.[25] They concluded that nerve-sparing was not associated with higher rates of (+) SMs or biochemical recurrence (BCR). The "trifecta" of continence, potency, and freedom from recurrence was achieved in 23% in their series.[25] Shikanov *et al*. reported significantly lower (+) SM rates in the mid- and posterolateral (+) SM location in extrafascial NVB sparing group compared to interfascial NVB sparing group in their series.[26] In a series of 35 patients with pT3 PCa patients, Casey *et al*. reported that bilateral or unilateral NVB sparing was not associated with increased (+) SMs.[27] In a single surgeon series of 500 RARPs performed by Yee *et al*. for patients with palpable disease on rectal examination, the (+) SM rate was detected as 9.9% (7.7% in cT2 and 26.3% in cT3 disease) and none of the (+) SMs were detected along the NVB.[28] In other series, unilateral and bilateral NVB sparing procedures have been reported in 15%–60% and 18%–58% of cases, respectively in patients with HRPC who underwent RARP in the literature.[25,29,30]

Although some authors have suggested preserving NVBs in preoperatively potent patients with IIEF-5 score of ≥5,[28] it is our policy to preserve NVBs regardless of the preoperative IIEF-5 score whenever technically possible depending on the intraoperative findings and tissue characteristics that is expected to have an impact on the postoperative urinary continence, too.

In summary, preservation of NVBs might be possible and safe during performing RARP in HRPC patients, which depends on patient factors and tissue characteristics.

LIMITS AND TECHNIQUE OF EXTENDED PELVIC LYMPH NODE DISSECTION DURING ROBOT-ASSISTED RADICAL PROSTATECTOMY

Currently, ePLND rather than standard pelvic LN dissection (sPLND) is recommended during RARP.[31] It has been reported that lymphatic drainage of the prostate is not limited to the obturator and external iliac LNs,

and an ePLND including the internal iliac, external iliac and obturator LNs increases LN yield that is expected to improve detection of LN metastasis.[21] Performing ePLND during RARP was suggested to carry the advantages of diagnostic and therapeutic benefits in patients with intermediate- or high-risk PCa.[32,33]

Borders of ePLND during RARP include:

1. Lateral border: genitofemoral nerves, psoas muscles, and ureters
2. Medial border: cut edge of the endopelvic fascia over the NVBs, internal iliac vessels
3. Superior border: common iliac arter and vein and presacral area
4. Inferior border: node of Cloquet, circumflex iliac vein.

In our technique, we initially identify the ureter on both sides in the pelvis, incise the peritoneum overlying it and dissect it until its crossing over common iliac artery. We perform ePLND after the completion of prostatectomy and before performing vesico-urethral anastomosis. We remove all the lymphatic tissue surrounding the major vessels and their tributaries. Before starting the ePLND procedure, we decrease the intra-abdominal carbon dioxide pressure to 10 mmHg in order to better identify and see particularly the veins. We use monopolar or bipolar coagulation in addition to polymer or metal endoclips for the ligation of small vessels and lymphatics.

In our experience with robot-assisted laparoscopic radical cystectomy for bladder cancer, we demonstrated that ePLND up to the inferior mesenteric artery could be efficiently performed with sufficient LN yields.[34,35] Therefore, we apply the same technique for performing ePLND when we perform ePLND is RARP for HRPC. Regarding RARP, obtaining a minimum of 20 LNs was suggested to be removed for ePLND.[36,37] On the other hand, LN yield has been suggested to depend on both surgeon and pathologist.[38,39] In addition, a wider anatomic dissection during ePLND was reported to lead to a greater total LN yield and a higher rate of LN metastases.[37,40,41]

Performing ePLND before the removal of the prostate might be another option that allows the surgeon to send LNs for intraoperative frozen section analysis. Montorsi stated that if metastases are found, reinspection of the area could be carried out in order to make sure if complete LN dissection has been obtained.[42]

ROLE OF PREOPERATIVE PROSTATE MAGNETIC RESONANCE IMAGING

Due to the European Society of Urogenital Radiology guidelines, recommended use of magnetic resonance imaging (MRI) in PCa consists of multi-parametric MRI (mp-MRI) that includes a combination of high-resolution T2-weighted images (T2WI), and at least two functional MRI techniques leading to better characterization than T2WI with only one functional technique.[43] Although T2WI MRI mainly assesses anatomy of the prostate, diffusion weighted imaging and MR spectroscopic imaging (MRSI) specify lesion characterization.[43] On the other hand, dynamic contrast enhanced MRI has a higher sensitivity in PCa detection.[43] It was reported that mp-MRI can be helpful in NVB sparing and continence sparing surgery and for detecting minimal extra-capsular disease.[43] In addition, MRSI with T2WI was suggested as very helpful in both excluding and detecting high-grade cancers of >0.5 cc in volume.[44,45]

Criteria for extra-capsular extension include irregularity and NVB thickening; bulge, loss of capsule and the capsular enhancement; measurable extra-capsular disease; obliteration of the recto-prostatic angle. Expansion; low T2 signal intensity; filling in of the prostate–SV angle; enhancement and impeded diffusion are regarded as the criteria for SV infiltration.

Although endorectal coil MRI was regarded as the state-of-the-art for staging PCa, it also has the disadvantages of increased cost and patient acceptability,[43] Brajtbord *et al.* reported that it has limited clinical ability to preoperatively predict pT3 PCa at RARP.[46]

Evaluation of preoperative digital rectal examination findings, high-resolution MRI findings, intraoperative tissue findings and erectile function status of the patient were suggested to guide NVB sparing at RARP.[47]

ROLE OF PREOPERATIVE PROSTATE BIOPSY

Currently, systematic transrectal ultrasound (TRUS) guided prostate biopsy (TRUS-Bx) is frequently used for the diagnosis of PCa. However, this technique has been reported the following disadvantages including poor identification of PCa with TRUS, detection of low-risk disease that might be suitable for active monitoring, misclassification of PCa compared to postoperative whole-mount pathologic evaluation.[48–50] A recent study compared the diagnostic efficacy of the MRI pathway with TRUS-Bx and found out that mp-MRI/magnetic resonance (MR)-guided biopsy reduced the detection of low-risk PCa and reduced the number of men requiring biopsy while improving the overall rate of detection of intermediate/high-risk PCa.[50]

OPEN VERSUS ROBOTIC RADICAL PROSTATECTOMY IN HIGH-RISK PROSTATE CANCER

Increasing number of publications exist in the literature comparing the outcomes of open versus robotic RP in HRPC. All of these studies are retrospective and no prospective, randomized study exists currently. Patients with neoadjuvant anti-androgen or hormonal therapy were excluded in these studies. Although patient characteristics of the study groups were similar in these retrospective studies, an inevitable bias exists related to patient selection that could not be controlled. Another important point is that more than one surgeon was involved for the study groups that might also lead to lack of uniformity but also reflects more than one surgeon's experience.[51] Therefore, the results should be interpreted with caution, and strict conclusions should not be made at present.

Outcomes of selected published papers comparing open versus robotic RP in HRPC patients are summarized in **Table 2**.[51–54] SM positivity,[51–56] BCR[52,55] and biochemical recurrence-free survival (BCRFS) rates,[53,54] additional cancer therapy[56] and oncologic outcomes[57] were all reported to be similar in studies comparing open versus robotic RP in the surgical management of HRPC. Although the number of patients was limited, Smith *et al*. reported similar (+) SM rates in their open versus robotic RP series of HRPC patients (58% and 56.3%, respectively; $P = 0.08$).[58]

Harty *et al*. included 153 and 152 patients in open and robotic RP groups, respectively in a retrospective study.[51] (+) SMs were detected in 15% and 12% of the patients with pT2 stage in open and robotic groups, respectively ($P > 0.05$). (+) SMs were detected in 74% and 79% of the patients with pT3 stage in open and robotic groups, respectively ($P > 0.05$). Pierorazio *et al*. included 743 and 105 patients in open and robotic RP groups, respectively in a retrospective study.[52] (+) SMs were detected in 5.7% and 8.3% of the patients with pT2 stage in open and robotic groups, respectively ($P > 0.05$).

Wambi *et al*. from the Vattikuti Urology Institute in USA evaluated the oncological outcomes of 368 patients with specimen Gleason 8 and 9 HRPC who underwent RARP. Mean overall BCRFS was 36% at 60 months. Regarding Gleason 8 and Gleason 9 PCa groups, BCRFS rates were reported as 47% and 21%, respectively ($P < 0.001$). In patients with extraprostatic extension (pT3a) with Gleason

Table 2: Outcomes of selected published papers comparing open versus robotic radical prostatectomy in HRPC patients

	Harty et al.[51]			*Pierorazio et al.*[52]			*Punnen et al.*[53]			*Busch et al.*[54]		
	ORRP	*RARP*	*P*	*ORRP*	*RARP*	*P*	*ORRP*	*RARP*	*P*	*ORRP*	*RARP*	*P*
Year	2013			2013			2013			2014		
n	153	152		743	105		177	233		110	110	
pT (%)												
pT2	24	22	-	33.2	34.3	NS	53	55	NS	36.4	46.4	NS
pT3	70	74	-	55.7	61.9	NS	43	43	NS	pT3a 21.8	pT3a 28.2	NS
pT4	6	4	-	-	-	-	4	2	NS	pT3b/pT4 29.1	pT3b/pT4 14.5	NS
(+) SM (%)	52.9	50	NS	29.3	34.3	NS	23	29	NS	42.7	40.9	NS
(+) SM by pT (%)												
pT2	15	12	NS	5.7	8.3	NS	-	-	-	-	-	-
pT3	74	79	NS	-	-	-	-	-	-	-	-	-
pT4	11	9	NS	-	-	-	-	-	-	-	-	-
LND performed (%)	58	56	NS	99.2	97.1	-	96	63	<0.01	97.3	94.5	NS
LN metastasis (N1) (%)	2.6	3.3	NS	10.8	3.8	-	15	4	<0.01	2	1.5	NS
Median LN count	-	-	-	8	6	NS	15	11	<0.01	9	6	0.037
BCR-free survival (%)	-	-	-	56.3	67.8	NS	84 at 2 years 68 at 4 years	79 at 2 years 66 at 4 years	NS NS	54.1 at 3 years	41.4 at 3 years	NS
LOS	-	-	-	-	-	-	1.85	1.62	<0.01	-	-	-
EBL	-	-	-	-	-	-	484	217	<0.01	-	-	-
Transfusion (%)	-	-	-	-	-	-	5	0	<0.01	-	-	-
NVB sparing	-	-	-	-	-	-				-	-	-
None (%)	-	-	-	-	-	-	8	2	<0.01	-	-	-
Unilateral (%)	-	-	-	-	-	-	58	44	<0.01	-	-	-
Bilateral (%)	-	-	-	-	-	-	34	54	<0.01	51.8	58.2	NS

ORRP: open radical retropubic prostatectomy; RARP: robot-assisted laparoscopic radical prostatectomy; N: number of patients; pT: pathologic stage; (+) SM: positive surgical margin; LN: lymph node; LND: lymph node dissection; BCR-free: biochemical recurrence-free; NR: not reported; NS: not significant; LOS (mean): length of hospital stay (days); EBL (mean): estimated blood loss (ml); NVB: neurovascular bundle; PCa: prostate cancer; HRPC: high-risk PCa

8 and Gleason 9 PCa groups, BCRFS rates were detected as 52% and 21%, respectively at 5 years ($P = 0.012$). LN invasion, specimen Gleason score, pathological stage, and tumor volume were identified as predictors of BCRFS on multivariate analysis.[59]

Although LN dissection was performed in a similar way in both open versus robotic RP series,[51–54] some authors such as Punnen *et al*. reported significantly lower LN yields thus reported lower LN metastasis rates in the RARP group.[53] While some authors reported similar LN yields,[52] some others reported inferior counts in the RARP groups.[53,54] In a systematic review by Yuh *et al*., it was stated that variability existed for the template of LN dissection, although ePLND improved staging and removed a higher number of metastatic nodes.[47] Silberstein *et al*.[55] stated that surgeons performing RARP were up to 5 times more prone to omit performing pelvic LN dissection compared to surgeons performing ORP even in HRPC patients due to the published literature.[60,61] Lower rates of LN dissections and LN yields in the RARP publications might be secondary to the learning curve of robotic surgeons and LN dissection policy of the institution. As an example, we perform ePLND in intermediate- or high-risk PCa patients and in those with an at least 5% risk of pelvic LN involvement by PCa according to Partin's tables.[20] On the other hand, Silberstein *et al*. performed ePLND in all of their patients with a 2% or greater risk of LN involvement assessed due to an established preoperative nomogram.[55] Particularly in low-risk PCa patients, ePLND was not performed in many RARP series due to these criteria on which debate is still ongoing.

Regarding complications, Gandaglia *et al*. reported similar complication rates between the two surgical treatment modalities.[56] As expected, less blood loss[53] and lower rates of blood transfusions[56] were reported in the RARP group compared to ORP in HRPC patients. Likewise, shorter duration of hospital stay was also detected in the RARP group.[56]

Rogers *et al*. evaluated the outcomes of RARP in a series of 69 elderly (≥70 years) patients.[62] Median duration of hospital stay was 1 day. Final pathologic examination revealed organ-confined disease with (−) SMs, and extra-capsular extension with (−) SMs were detected in 37.7% and 39.1% of the patients, respectively. There were only four complications (5.8%) which included urine leak and ileus in two patients each, respectively. At a median follow-up of 37.7 months, BCR occurred in 17.4% of the patients. Actuarial BCRFS was detected as 91% at 12 months and 86% at 36 months. At a median follow-up of 26.2 months, 81.5% of the patients was using no pad or 1 pad per day and 33.3% of the patients with preoperative SHIM score >21 achieved erections for sexual intercourse. Due to their experience, RARP in elderly patients with HRPC was regarded as a safe and feasible minimally invasive surgical procedure with good intermediate oncologic and functional outcomes.[60]

Technique and extent of NVB sparing were not mentioned clearly in most of the publications. Punnen *et al*. stated that complete bilateral NVB sparing was performed more often in the RARP group in their series.[53] Extent of NVB sparing might be expected to have an impact on the functional outcomes including urinary continence and erectile function. However, functional outcomes have not been reported in most of the literature comparing open versus robotic RP in HRPC patients, which needs further research.

In summary, RARP seems to have similar oncologic outcomes including (+) SM rates

and LN yields with similar complication rates compared to open surgery in HRPC patients. In addition, decreased blood loss, lower rates of blood transfusion and shorter duration of hospital stay seem to be the advantages of robotic surgery in this patient group.

ONCOLOGIC OUTCOMES FOLLOWING ROBOT-ASSISTED RADICAL PROSTATECTOMY AT HIGH-RISK PROSTATE CANCER PATIENTS

Lymph node yield, (+) lymph node rate and (+) surgical margin rates

In **Table 3**, LN yield, (+) LN rates and (+) SM rates of selected HRPC series treated with RARP and ePLND are summarized.[29,52,53,55,63–66] In the literature, not all of the published papers stated whether LN dissection was performed limited or extended in HRPC patient who underwent RARP. Therefore, we selected papers that stated ePLND was performed (**Table 3**). Due to this table, LN yield ranged between 6 and 24, (+) LN rate ranged between 3.8% and 33.3% and (+) SM rate ranged between 12.0% and 48.8%.

Yuh *et al*. from The City of Hope National Cancer Center in USA evaluated outcomes of 143 intermediate- and high-risk PCa patients whom they performed robotic ePLND following RARP.[65] Operative time for bilateral ePLND was between 30 and 45 min and median blood loss was 200 ml. No patient required blood transfusion. Average length of follow-up was 7 months in their series. Symptomatic lymphocele formation was detected in 3%, although routine pelvic imaging in the postoperative period was not performed. Therefore, the incidence of asymptomatic lymphocele might be higher in their series. They concluded that robotic ePLND can be performed safely with nodal yields >20.[65]

Liss *et al*. evaluated the outcomes and complications of patients who underwent sPLND and ePLND, or who did not undergo pelvic LN dissection (non-PLND) during RARP. When they examined ePLND ($n = 41$) and sPLND ($n = 57$) in only HRPC patients, mean LN yields were detected as 20 and 17, respectively ($P = 0.048$). In addition, (+) LN rates were detected as 29.3% and 12.3%, respectively ($P = 0.042$). Complication rates for all groups were similar. Lymphocele formation rates were 5% and 2.5%, respectively. They concluded that robotic ePLND improved LN yield and the proportion of LN metastases identified in HRPC patients.[67]

Jung *et al*. evaluated the outcomes of ePLND in HRPC patients.[66] They detected that 25% of (+) LNs were in the internal iliac and common iliac packets. In addition to the (+) internal iliac LNs, 75% of nodes were found in that location, exclusively. They concluded that ePLND including internal iliac packet should be performed during RARP in HRPC cancer that provided accurate pathologic staging and might have a survival benefit.[66]

Davis *et al*. from The University of Texas, MD Anderson Cancer Center, Houston stated that ePLND is feasible during RARP that increases LN yield and (+) LN rate particularly in HRPC patients. Due to their experience, median operative duration for ePLND was 42 min that was roughly double that of a sPLND. They suggested extensive clipping in order to avoid postoperative lymphoceles.[68]

Bmiochemical recurrence and recurrence-free survival

Silberstein *et al*. compared early oncologic outcomes of 961 ORP and 493 RARP patients.[55] Median follow-up for patients without BCR was 1-year and 0.7 year, respectively for ORP and RALP groups. In a multivariate analysis model adjusting for preoperative risk, no significant difference was detected in BCR rates between the groups. When National Comprehensive Cancer Network risk was used in place of nomogram risk, the results were similar. The 2-year probability of recurrence was 22.4% for HRPC patients in ORP group and was 15.2% in RARP group ($P > 0.05$). They concluded that open and robotic RP had similar early oncological outcomes in patients with HRPC.[55]

In a series of 233 HRPC patients, Punnen *et al*. reported recurrence-free survival at 2 years and 4 years as 79% and 66%, respectively after RARP.[53] Pierorazio *et al*. reported BRFS at 3 years as 67.8% in a series of 105 HRPC patients who underwent RARP.[52] In another study, mean 3-year recurrence-free survival was reported as 41.4% for 110 HRPC patients who underwent RARP and mean estimated 3-year overall survival was 95.4%.[54] In a series of 112 HRPC patients who underwent RARP, after a median follow-up of 13 months, Lavery *et al*. reported BCR in 20% of the patients.[25]

Presence of LN metastasis,[66] serum PSA level, clinical stage and pathologic grade[69] were detected to be associated with BCR following RARP in HRPC patients.

OPERATIVE AND PERIOPERATIVE PARAMETERS – INTRAOPERATIVE ESTIMATED BLOOD LOSS, OPERATION TIME AND DURATION OF HOSPITAL STAY

In the published literature mean operative time ranged between 111 and 214 min;[25,29,62–66] mean estimated blood loss (EBL) ranged between 84 and 432 ml[25,29,62–66] and mean duration of hospital stay ranged between 1 and 5.8 days[25,29,62–66] in selected papers that evaluated RARP outcomes in HRPC patients.

The number of papers comparing operative and perioperative parameters including EBL, operation time and duration of hospital stay are very limited in the published literature. Punnen *et al*. reported significantly less EBL (200 *vs* 400 ml, $P < 0.01$) in the robotic group in a retrospective comparison of 177 ORP and 233 RARP in HRPC patients.[53] In another retrospective study, Gandaglia *et al*. reported significantly lower rates of blood transfusion and shorter duration of hospital stay in the robotic group when compared to open surgery in patients with HRPC.[56]

COMPLICATIONS

Gandaglia *et al*. evaluated if RARP was safe in HRPC patients.[56] They included 1512 patients with HRPC patients within the Surveillance, Epidemiology, and End Results Medicare-linked database diagnosed between 2008 and 2009. Overall, 706 (46.7%) and 806 (53.3%) patients underwent ORP and RARP, respectively. Following propensity-matched analyses, 706 patients

Table 3: LN yield, (+) LN rate and (+) SM rate of selected HRPC series with stage pT2 disease treated with RARP and ePLND[47]

Study	*Year*	*n*	*LN yield*	*(+) LN rate (%)*	*(+) SM rate (%)*
Jayram *et al*.[29]	2011	148	15	12.3	20.9
Pierorazio *et al*.[52]	2013	105	6	3.8	34.3
Punnen *et al*.[53]	2013	233	11	4.0	29.0
Silberstein *et al*.[55]	2013	493	15	8.0	15.0
Ham *et al*.[63]	2009	121	19	24.0	48.8
Sagalovich *et al*.[64]	2013	83	13	13.4	12.0
Yuh *et al*.[65]	2012	30	22	33.3	26.7
Jung *et al*.[66]	2012	200	24	22.0	41.5

N: number of patients; LN: lymph node; (+) SM: positive surgical margin; ePLND: extended pelvic lymph node dissection; PCa: prostate cancer; HRPC: high-risk PCa; RARP: robot-assisted laparoscopic radical prostatectomy

remained. Due to their study, no differences were observed in complications between the two groups (30% and 28.3%, respectively in open *vs* robotic RP patients, $P = 0.6$). They stated that their finding persisted despite adjusting for tumor and patient characteristics in addition to hospital clustering. They also compared two groups for prediction of specific complication schemes that also showed no difference.

Other authors reported complication rates between 4% and 30% in HRPC patients who underwent RARP.[29,62,63,65] Due to these studies, lymphocele, ileus, anastomotic leakage, deep vein thrombosis and rectal injury were among the reported complications. Ham *et al*. reported rectal injury rate as 1.7%.[63] Lymphocele formation was reported between 2.5% and 6.6% in other studies.[63,65] Although not all authors have reported their complication rates and type of complications in detail in the literature, due to the published series, RARP in HRPC patients seems to be a safe procedure with acceptable complication rates.

FUNCTIONAL OUTCOMES – URINARY CONTINENCE AND ERECTILE FUNCTION

Functional outcomes following RARP include urinary continence and erectile function. In the published literature, only very few authors have reported their functional outcomes following RARP in HRPC patients. In a systematic review by Yuh *et al*., 1-year urinary continence (0–1 safety pad per day) rate ranged between 78% and 95% and erectile function recovery ranged between 52% and 60%.[47] Yee *et al*. reported their 1-year pad-free continence rate as 84% in HRPC patients who underwent RARP.[28] Preoperative erectile function status of the patient, postoperative adjuvant treatment requirement, NVB sparing (unilateral or bilateral), bladder neck preservation and urethral length should all be considered seriously in the evaluation of postoperative functional outcomes.

Rocco *et al*. suggested that restoration of the posterior aspect of the rhabdosphincter following ORP leads to substantial and significant reduction in time to early continence with no adverse effects.[70] Likewise, Rocco *et al*. confirmed same findings in a series of patients who underwent laparoscopic RP.[71] Others such as Simone *et al*. also reported outcomes supporting their outcomes.[72] However, due to the experience of Joshi *et al*.,[73] posterior reconstruction of the musculofascial complex was not found to improve early urinary incontinence after RARP. Ficarra *et al*. reported that recent systematic reviews of the literature showed only a minimal advantage in favor of posterior musculofascial reconstruction regarding urinary continence recovery.[74] They suggested performing posterior musculofascial reconstruction during RARP and described it as a simple, reproducible and safe surgical step that could be performed without significantly increasing operation time. In addition, they suggested that it might improve hemostasis and serve as a support for the urethra-vesical anastomosis.[74]

LEARNING CURVE AND SURGEON'S EXPERIENCE

No specific paper exists in the literature in terms of learning curve of RARP in HRPC patients. It was reported that outcomes of RP in open series were driven by experience of the surgeon.[38,52,75] Others also stated that increasing surgeon experience in addition to improvement of the surgical technique used decrease (+) SM rates in ORP.[76–78] Therefore, greater surgical volume and experience are expected to lead to better outcomes that might also apply to RARP in HRPC patients.

In conclusion, RARP seems to have similar oncologic outcomes including (+) SM rates, BCR rates, BCRFS rates, postoperative adjuvant therapy requirement rates and LN yields with similar complication rates compared to open surgery in HRPC. In addition, decreased blood loss, lower rates of blood transfusion and shorter duration of hospital stay seem to be the advantages of robotic surgery in this particular patient group. Tissue and tumor characteristics might be different in HRPC patients compared to low-risk group that needs increased surgical experience during performing RARP. RARP in HRPC patients seems to be safe and technically feasible with good intermediate-term oncologic results, acceptable morbidities, excellent short-term surgical and pathological outcomes and satisfactory functional results.

EDITORIAL COMMENT—(BY DR JOHN W DAVIS, DEPARTMENT OF UROLOGY, THE UNIVERSITY OF TEXAS, MD ANDERSON CANCER CENTER, HOUSTON, TEXAS, USA)

Prostate cancer is known to be one of the slowest growing solid tumors, and the lower end of grade and volume rarely threatens mortality during normal human longevity. Therefore, novel treatments for PCa can "look good" by selecting more favorable risk patients to treat. However, radical prostatectomy technique variations have one unique advantage – the full pathology report. Therefore, in the evolution of novel techniques in RP, the laparoscopic and now robot-assisted techniques can go through a reasonable learning curve in low-intermediate risk disease, but then move on to high-risk disease, which is likely the greater threat to the average patient diagnosed. Canda and Balbay review the literature with comments on the key techniques of robotic prostatectomy in high-risk disease with attention to key outcomes. At MD Anderson Cancer Center, approximately 15% of our high-risk patients taken for surgery are high-risk and are routinely performed with robot assistance – often with the involvement of a clinical trial of neoadjuvant therapy.

COMPETING INTERESTS

All authors declare no competing financial interests.

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